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Amendment and Response

Serial No.: 10/038,984

Confirmation No.: 9705

Filed: January 4, 2002

For: COMPOSITION AND METHOD FOR IN VIVO AND IN VITRO ATTENUATION OF GENE
EXPRESSION USING DOUBLE STRANDED RNA**Remarks**

The Office Action mailed April 20, 2006, has been received and reviewed. The pending claims are claims 1-7, 15-19, 22, 27-32, 39, 48, 62, 63, 72-76 and 78-81. Reconsideration and withdrawal of the rejections are respectfully requested.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 1-7, 15-19, 22, 28-32, 39, 62, 63, 72-76 and 78-81 under 35 U.S.C. §102(e) as being anticipated by Fire et al. (U.S. Patent No. 6,506,559). The applicants note the text of this rejection is nearly identical to the rejection made in the Office Action dated September 8, 2004. This rejection is respectfully traversed.

"In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure' " (M.P.E.P. §2121.01). The applicants respectfully assert that Fire et al. does not provide an enabling disclosure for embryonic zebrafish cells (independent claims 1, 48, 63, and 81) or vertebrate cells (independent claim 75). Mere passing reference to embryonic stem cells (col. 9, lines 44-48), zebrafish (col. 8, lines 35-37) and vertebrates (col. 8, lines 35-37) does not enable the attenuation of gene expression in embryonic zebrafish cells or vertebrate cells, any more than Fire et al.'s listing of over 100 types of cancer on column 10, line 28 to column 11, line 4 provides an enabling disclosure for cancer treatment. The only detailed description of work done by Fire et al. was in *C. elegans*. This does not provide an enabling disclosure for embryonic zebrafish cells or vertebrate cells. Not only is *C. elegans* an invertebrate, but it is a primitive and simple invertebrate. It is only 1 mm long, includes only 959 somatic cells, and is often handled as a microorganism; for example, it is usually grown on petri plates seeded with bacteria. The description of dsRNA administration to this single, simple, invertebrate organism does not provide an enabling disclosure for the claimed methods in embryonic zebrafish cells or vertebrate cells.

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Fire, a leading researcher in the field, expressed doubt about the applicability of this technology to vertebrates. In a review published *subsequent to the filing* of U.S. Patent No. 6,506,559, Fire stated:

"[f]rom a technical perspective, one could certainly *hope* that RNA-triggered silencing would exist in vertebrates Although this hope is not ruled out by any current data, *the simple protocols used for invertebrate and plant systems are unlikely to be effective.*" (Fire, Trends in Genetics, 15:358-363, 363 (1999); emphasis added)

The present inventors were the first, in this highly competitive art area, to demonstrate success in attenuating gene expression in target vertebrate cells using dsRNA. Indeed, the state of the art suggested that dsRNA could *not* be successfully used for specific attenuation of gene expression in vertebrates. Gene silencing technology based on dsRNA, as it relates to vertebrates, was not in the hands of the public until the present inventors developed a method that truly caused attenuation of gene expression in a vertebrate system. Thus, while the use of dsRNA to attenuate target gene expression in vertebrates is nominally disclosed in U.S. Patent No. 6,506,559, the teachings of U.S. Patent No. 6,506,559 are insufficient to anticipate the claimed invention.

Furthermore, with respect to those claims reciting "*in vivo*," (independent claims 1, 48, 63, and 81), the prosecution history of Fire et al. shows Fire et al. does not provide an enabling disclosure. The Examiner is requested to note that during prosecution of the application that eventually issued as Fire et al., the Patent Office rejected several claims of Fire et al. under 35 U.S.C. §112, first paragraph, for lack of enablement, stating "the specification, while being enabling for methods of inhibiting expression of a target gene using a double stranded RNA in nematode or in vitro, does not reasonably provide enablement for methods of inhibiting expression of a target gene using a double stranded RNA in any organism in vivo (whole organism)" (page 6, first paragraph, of the Office Action dated February 14, 2001). This rejection was not overcome by Fire et al., and independent claim 1 was later amended by Fire et al. to recite "*in vitro*" (see Response dated January 8, 2002, page 5, fourth paragraph). Thus,

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according to the prosecution history, the Office has concluded that Fire et al. "does not reasonably provide enablement for methods of inhibiting expression of a target gene using a double stranded RNA in any organism in vivo (whole organism)." Since Fire et al. does not contain an enabling disclosure, it cannot be used to reject the present claims under 35 U.S.C. §102(e).

For at least these reasons, reconsideration and withdrawal of the present rejection is respectfully requested.

The 35 U.S.C. §103 Rejection

The Examiner rejected claims 1-7, 15-19, 22, 27-32, 39, 48, 62, 63, 72-76 and 78-81 under 35 U.S.C. §103(a) as being unpatentable over Fire et al. (U.S. Patent No. 6,506,559), in view of Kreutzer et al. (U.S. Patent Publication No. 2005/0100907). This rejection is respectfully traversed.

The Examiner is requested to note that Kreutzer et al. is not prior art, and therefore cannot be used in the present rejection. "A 35 U.S.C. 103 rejection is based on 35 U.S.C. 102(a), 102(b), 102(e), etc. depending on the type of prior art reference used and its publication or issue date." (M.P.E.P. §2141.01). Kreutzer et al. was filed July 2, 2003, and published May 12, 2005. It is a continuation of a U.S. application (filed on September 17, 2001), which was a national stage application of PCT/DE00/00244371 (filed on January 29, 2000). The PCT application claims priority to two foreign applications. "For U.S. application publications of applications that claim the benefit under 35 U.S.C. 120 or 365(c) of an international application filed prior to November 29, 2000, apply the reference under 35 U.S.C. 102(e) as of the actual filing date of the later-filed U.S. application that claimed the benefit of the international application" (M.P.E.P. §2136.03 (II)(c)(3)). The actual filing date of Kreutzer et al. is September 17, 2001, thus, the 102(e) date of Kreutzer et al. is September 17, 2001. The present application is a continuation of U.S. 09/493,301, which was filed January 28, 2000.

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The Examiner asserted that the claims are obvious in view of the combination of Fire et al. and Kreutzer et al. (Office Action at page 5, last paragraph). Since Kreutzer et al. is not prior art, the Examiner has failed to present a prima facie case of obviousness.

For at least this reason, reconsideration and withdrawal of the present rejection is respectfully requested.

Summary

It is respectfully submitted that the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted

By

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By: David L. Provence
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CERTIFICATE UNDER 37 CFR §1.8:

The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 20 day of Sept, 2006, at 3:20 pm (Central Time).

By: Sandy Truehart
Name: Sandy Truehart